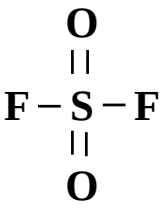
# SULFURYL FLUORIDE (Vikane®)

# RISK CHARACTERIZATION DOCUMENT



## Executive Summary (DRAFT)

**Medical Toxicology Branch**
**Worker Health and Safety Branch**
**Environmental Monitoring Branch**
**Department of Pesticide Regulation**
**California Environmental Protection Agency**

**June 2005**

## LIST OF CONTRIBUTORS AND ACKNOWLEDGEMENT

This Risk Characterization Document (RCD) addresses the inhalation exposure to sulfuryl fluoride as Vikane®, used in structural fumigation and non-food commodity fumigation. It is consisted of five documents: Executive Summary, Volume I. Health Risk Assessment, Volume II. Occupational and Residential Exposure Assessment, Volume III. Environmental Fate, and Volume IV. DPR Responses to Comments.

**Executive Summary**

Author: Lori O. Lim, Ph.D., D.A.B.T., Staff Toxicologist
Health Assessment Section
Medical Toxicology Branch

**Volume I. Health Risk Assessment**

**Author:** Lori O. Lim, Ph.D., D.A.B.T., Staff Toxicologist
Health Assessment Section
Medical Toxicology Branch

**Volume II. Occupational and Residential Exposure Assessment**

**Authors:** Roger Cochran, Ph.D., D.A.B.T., Staff Toxicologist
Donna DiPaolo, Ph.D. Associate Toxicologist*
Worker Health and Safety Branch
(*no longer with the Department)

**Volume III. Environmental Fate**

**Author:** Wynetta S. Kollman, Ph.D.
Associate Environmental Research Scientist
Environmental Monitoring Branch

**Volume IV. DPR Responses to Comments**

**Author:** Department of Pesticide Regulation Staff

**Acknowledgement:**

The authors acknowledge the review of a March 2004 draft of this RCD by the Office of Environmental Health Hazard Assessment (OEHHA) and the Air Resources Board (ARB) of the California Environmental Protection Agency. An August 2004 draft was reviewed by Dr. Roger Atkinson and Dr. Craig Byus, AB 1807 Scientific Review Panel lead reviewers for this compound. This version was also provided to OEHHA and ARB, as well as posted for public comment under the mandate of AB 1807.

## TABLE OF CONTENTS

## Introduction

The Department of Pesticide Regulation (DPR) conducts risk assessments for pesticides used in California to determine if the use poses a present or potential human health hazard in California. Risk assessment is the systematic scientific characterization of potential adverse health effects resulting from human exposures to hazardous agents or situations. This type of assessment includes a quantitative assessment of the exposure and the potential magnitude of the risks, and a description of the uncertainties in the conclusions and estimates. After the completion of the risk assessment, the risk management phase takes place at DPR. Risk management refers to the process by which policy actions are chosen to deal with hazards identified in the risk assessment process. Risk managers consider scientific evidence and risk estimates, along with statutory, engineering, economic, social, and political factors, in evaluating alternative regulatory options and choosing among those options.

Risk assessments are mandated by Senate Bill (SB) 950, the Birth Defect Prevention Act, and Assembly Bills (AB) 1807 and 3219. Under SB 950, the risk assessment is comprehensive and considers the potential exposures of various population groups, which may include workers, residents, and bystanders, depending on how the pesticide is used. For each group, multiple routes of exposure, when appropriate, are assessed. These include inhalation via the air, absorption through the skin, and consumption of treated food. In comparison, AB 1807 and 3219 establishes a procedure for identification and control of toxic air contaminants (TACs) in California. The statutes defines toxic air contaminants as air pollutants that may cause or contribute to an increase in mortality or in serious illness, or that may pose a present or potential hazard to human health. DPR TAC program focuses on the evaluation and control of pesticides in ambient community air.

This report describes the risk assessment for the inhalation exposure to sulfuryl fluoride in the product Vikane®, under both SB 950 and AB 1807 mandates. In preparing this report, DPR staff reviewed pertinent scientific literature and reports through Spring 2005. Based on the results of this comprehensive evaluation, the Director of DPR will determine whether sulfuryl fluoride is a TAC, and whether mitigation measures are needed to reduce the exposure by workers and the general population in California. If sulfuryl fluoride is designated a TAC, the risk management provisions of the law mandate the DPR to determine the need for and develop appropriate control measures for sulfuryl fluoride uses-in consultation with the Office of Environmental Health Hazard Assessment (OEHHA), the Air Resources Board (ARB), the air pollution districts, air quality management districts, and county agricultural commissioners of the affected counties.

## What is contained in this report?

This report evaluates the potential for sulfuryl fluoride exposure and includes:

- A review of the available scientific evidence on sulfuryl fluoride and fluoride regarding their physical properties, sources in the environment, and fates in the environment;
- Summary of toxicology studies conducted with sulfuryl fluoride and fluoride;

- Estimates of human exposure to sulfuryl fluoride in the air at work sites and surroundings; and
- An assessment of the risk to humans resulting from current or anticipated exposures to airborne sulfuryl fluoride.

**What is sulfuryl fluoride, what are the primary sources of sulfuryl fluoride in the environment, and how is it used?**

Sulfuryl fluoride is a colorless, odorless gas. The molecular formula is $F_2O_2S$ and the molecular weight is 102.1 g/mole. It is highly volatile with a vapor pressure of $1.16 \times 10^4$ mmHg at 25 °C and a Henry's Law Constant of $3.28 \times 10^{-2}$ atm·$m^3$/mol. It is soluble in water at 750 ppm (at 25 °C, pH 7), and readily soluble in most organic solvents.

The primary source of sulfuryl fluoride in the environment is from its use as a fumigant. Sulfuryl fluoride, marketed as Vikane®, is used to fumigate sealed structures and their contents (construction materials, furnishings, and household effects) such as dwellings (including mobile homes), buildings, barns, vehicles, fumigation chambers, rail cars, and surface ships in port. It controls existing infestations of insects and related pests such as drywood termites, powder post beetles, old house borers, death-watch beetles, bedbugs, cockroaches, clothes moths, rats, and mice.

In the preparation of a building for fumigation, the structure is evacuated and edible items are placed in airtight sealed containers. With windows and doors opened, the unoccupied building is covered with a tarpaulin (tarp) and sealed at the base to contain the fumigant. Since Vikane® is odorless and colorless, chloropicrin is added as a warning agent. On the next day, the tarpaulin is removed and the inside is actively aerated with fans for at least 1 hour, and later passively to disperse and release the fumigant into the atmosphere. After a minimum aeration of 8 hours, the sulfuryl fluoride air concentration at the breathing zone inside the building is measured. The building is approved or "cleared" when the concentration is 5 ppm or less, a level considered safe for residents and workers to reoccupy the buildings. Sulfuryl fluoride is also used in the fumigation of non-food commodities such as pallets, furniture, bags, beds, and mattresses. In this type of fumigation, sulfuryl fluoride is introduced into containers or chambers with the commodity to be fumigated. After fumigation, these chambers are aerated, with the release of sulfuryl fluoride via a stack into the atmosphere. For both types of fumigation, posting of a sign with information on the fumigation is required from application until the treated site air concentration is 5 ppm or less.

In California, the total pounds of sulfuryl fluoride used ranged from 1,502,091 pounds in 1993 to 3,042,882 pounds in 2002. The average annual use for this reporting period was 2,172,705 pounds. Sulfuryl fluoride is used in all California counties throughout the year.

**What are the fates of sulfuryl fluoride in the environment?**

After fumigation, sulfuryl fluoride in the air of treated structures is immediately released into the atmosphere in the gaseous state. Once in the atmosphere, the fate of sulfuryl fluoride is unclear since there are no available studies on this subject. It is entirely possible that sulfuryl fluoride has a long or very long atmospheric lifetime and should therefore, be considered a greenhouse gas.

There is a slower release of sulfuryl fluoride, which had adsorbed into structural material and household commodities (non-food). The rate of release depends on the type of material. Studies showed that sulfuryl fluoride is retained longer in synthetic material such as polystyrene insulation, latex baby bottle nipples, and polyester cushion fibers, compared to other materials.

**Who will be exposed to sulfuryl fluoride, and what are the exposure levels?**

There are three population subgroups, which may be exposed to sulfuryl fluoride: workers, residents, and bystanders. In this report, their exposures are expressed as absorbed doses, which accounts for differences in the age-related inhalation rate, and in the exposure duration under the various scenarios. For workers, their exposure durations are acute, short-term, intermediate-term, long-term, and lifetime. For residents and bystanders, the exposures are primarily acute and short-term durations. For each group, the highest exposure occurs with acute exposure.

For structural fumigation, the workers are designated as fumigators and tent crew. The fumigators introduce the fumigant into the structure, start aeration, and clear the building for reentry. They may have additional exposure when they perform tent crew activities. The tent crew seals the structure to prevent fumigant leakage during fumigation, and dismantles the tarp to aerate the structure after fumigation. The exposures of these workers were determined by monitoring studies that measured the air concentrations in the environment and breathing zones during typical fumigation of California homes using application rate lower than the maximum allowed on the label (submaximal rate). Under acute exposures, the range of estimated exposures was 1.17 mg/kg/day (fumigator doing both fumigator and tent crew activities) to 0.000006 mg/kg/day (fumigator checking structure after the first hour of aeration). The estimated exposures would be 14.5 times higher if the maximal rate application were used.

Non-food commodity fumigation involves the fumigators, and another category of workers, handlers. The handlers transfer commodities from the treatment site to a storage site or to the market. Currently there are no air monitoring data for non-food commodity handlers. The estimated exposures of these workers were based on an assumed exposure to a maximal sulfuryl fluoride air concentration of 5 ppm (0.43 mg/kg/day) because levels greater than this would required the use of self-contained breathing apparatus, according to the Vikane® label.

Residents of treated homes are exposed to sulfuryl fluoride after their houses have been treated because the current label permits reentry when the air concentration is no higher than 5 ppm. Data from a monitoring study involving 7 California homes were used to estimate these exposures. The data show that indoor air concentrations did not go to zero in 24 hours after aeration. During the first 24 hours after potential reentry, the mean sulfuryl fluoride air

concentrations in these houses range from 0.01 ppm to 1.58 ppm. This would be equivalent to an absorbed dose ranging from 0.20 mg/kg/day for 15-18 year olds to 0.57 mg/kg/day for infants <1 years old. At 40-48 hours after aeration, sulfuryl fluoride was still detected, ranging from 0.02 ppm to 0.48 ppm.

When fumigation or aeration occurs in a fumigated structure, bystanders, i.e., adult and child residents living nearby, have the potential for short-term exposure during their normal outdoor activities. As there are no data on the amount of sulfuryl fluoride, which may enter adjacent homes, indoor and outdoor air levels are assumed to be the same. Therefore, in addition to potential exposure during routine outdoor activities, bystanders may also be exposed while indoors. The estimated bystander exposures were derived from monitoring studies using a submaximal rate of application. For acute exposure during the application phase, the range of estimated absorbed doses ranged from 0.14 mg/kg/day (15 to 18 years old) to 0.36 mg/kg/day (infants <1 years old). The estimated acute absorbed doses during aeration using the Tarpaulin Removal and Aeration Plan method currently used in California ranged from 0.36 mg/kg/day (15 to 18 years old) to 0.90 mg/kg/day (infants <1 years old). The calculated exposures during application and aeration were 10 times higher if maximal rate application was used.

Bystanders near a non-food commodity fumigation facility may experience exposures during the application and aeration phases of the fumigation. As sulfuryl fluoride is rarely used to fumigate non-food commodities, only acute exposures are expected. As with structural fumigation, these bystanders are assumed to be exposed to sulfuryl fluoride while both outdoors and indoors at a maximum ambient air level of 5 ppm. For acute exposure, the range of estimated absorbed doses was 0.9 mg/kg/day (15 to 18 years old) to 2.3 mg/kg/day (infants <1 years old).

**What are the potential health effects from acute or repeated exposures to sulfuryl fluoride and fluoride?**

In humans, acute inhalation exposure to high concentrations of sulfuryl fluoride resulted in respiratory irritation, lung damage, central nervous system depression, and death. These high exposures occurred when people entered structures under fumigation illegally or after insufficient aeration. Epidemiological studies reported that fumigation workers who used sulfuryl fluoride showed neurological effects, which included reduced performance on cognitive tests and pattern memory tests, and reduced olfactory function. However, there were caveats to this study including: some workers were also exposed to methyl bromide, another neurotoxicant, and actual exposure levels and duration of the workers were not known.

Sulfuryl fluoride is acutely toxic at high concentrations in experimental animals. The concentrations for 50% lethality ($LC_{50}$) in rats are 3020-3730 ppm for 1-hour exposure and 991-1500 ppm for 4-hour exposure. The 4-hour $LC_{50}$ in mice is >400 ppm to 660 ppm. At non-lethal concentrations, neurotoxicity is observed in rats, mice, rabbits, and dogs.

With repeated exposures, the primary target tissues for sulfuryl fluoride inhalation toxicity in experimental animals were the brain, respiratory system, and teeth. Fluoride had been proposed as the active metabolite in the toxicity of sulfuryl fluoride. With up to two-weeks of exposure,

clinical signs observed included tremors, lethargy, respiratory effects, incapacitation, tetany, and convulsion. Animals treated with sulfuryl fluoride for two weeks showed tissue damage in the kidney (rats), brain (rabbits, mice), and respiratory tract (rabbits and dogs). After 13 weeks of inhalation exposure, the brain was the primary target for sulfuryl fluoride toxicity in all species studied (rats, mice, rabbits, and dogs). The most common lesion was vacuoles in the cerebral tissues. Other effects reported were nasal tissue inflammation (rats and rabbits), kidney hyperplasia (rats), lung histiocytosis (rats), thyroid hypertrophy (mice), and fluorosis (rats). The significant finding from reproductive and developmental toxicity studies was reduced body weight of fetuses (rabbits), pups (rat), and dams (rats). There were no teratogenic effects in rats or rabbits exposed to sulfuryl fluoride during gestation.

With chronic exposure, the primary target tissue for sulfuryl fluoride was the brain and the respiratory tract in rats, mice, and dogs. As with subchronic exposure, brain vacuoles were observed in the cerebrum. The sites of lesions in the respiratory tract included nasal tissues, trachea, larynx, and lungs. Dental fluorosis was observed in both rats and dogs. Progressive glomerulonephropathy was considered the cause of death in sulfuryl fluoride treated rats.

**Is there any potential cancer risk from exposure to sulfuryl fluoride?**

Sulfuryl fluoride is not considered a cancer-causing compound at this time. It did not cause tumors in rats and mice after lifetime exposures. Sulfuryl fluoride also did not cause any damage to the genetic material in laboratory studies.

**Does the concentration of sulfuryl fluoride in the air pose a potential health hazard for humans?**

While the current label limited the exposure to no higher than 5 ppm, this report shows that human exposures under some scenarios are higher than 5 ppm. One way to quantify the potential health hazard of human exposure is by comparing the No-Observed-Effect Level (NOEL), a dose does not cause toxicity in experimental animals, and the human exposure levels under different scenarios. This comparison yields a numerical term, known as a margin of exposure (MOE), the ratio of the NOEL in animals to the estimated exposure in humans. For sulfuryl fluoride, the NOELs for acute, 1-2 weeks, subchronic (13-weeks) exposures are 54 mg/kg/day, 7.2 mg/kg/day, 2.2 mg/kg/day, and 0.72 mg/kg/day. Based on the uncertainty in the toxicology database, scenarios with MOEs lower than 100 and 1000 for occupational and residential/bystander exposures, respectively, are considered to pose a health hazard for humans.

The hazard can also be quantified by comparing with the reference concentration, which is an estimate of a daily inhalation exposure concentration for the human population that is likely to be without an appreciable risk of deleterious non-carcinogenic effects. This term includes the consideration of the toxicity and uncertainties in its determination. The reference concentrations (and exposure durations) for workers are 2.57 ppm (acute), 0.48 ppm (1-2 weeks), 0.14 ppm (subchronic), and 0.04 ppm (chronic). For infants, the highest exposed group in the general population, the reference concentrations (and exposure durations) are 0.12 ppm (acute), 0.023

ppm (1-2 weeks), 0.007 ppm (subchronic), and 0.002 ppm (chronic). For the listing of a pesticide as a TAC under AB 1807, the exposure of bystanders is compared with the reference concentration. Exposures exceeding 1/10 of the reference concentration would be considered for listing as a TAC. This criterion is equivalent to a MOE of at least 10,000 for bystander exposures.

The risk assessment recommends that sulfuryl fluoride should be listed a TAC. Furthermore, the exposures of workers, residents, and bystanders under many scenarios pose health hazards and need to be reduced.

**Does fluoride ion, as a degradation product of sulfuryl fluoride, pose a potential health hazard?**

The sources of human exposure to fluoride are drinking water (major source), food, dental products, and use of fluoride-containing pesticides such as sulfuryl fluoride and cryolite. With low-level chronic exposures to fluoride, the primary effect is dental fluorosis. There is no clear evidence that fluoride causes cancer. Sodium fluoride caused damage to the genetic material under some laboratory conditions. Chronic toxicity studies with sodium fluoride in the drinking water showed low incidence of a type of bone cancer (osteosarcoma) in male rats, but not in female rats or either gender of mice. Another study with sodium fluoride in the diet showed increased incidences of osteomas (benign bone tumors) in mice, but not rats.

There is a potential human exposure to fluoride from the use of sulfuryl fluoride in Vikane®; however, it is not evaluated in this report due to lack of exposure data. This report provides estimates of fluoride exposure, which show a wide range depending on the assumptions. The inhalation and dietary exposures to fluoride will be evaluated when the risk assessment for ProFume® is conducted. ProFume® is a recently registered product to fumigate food commodities.